NAA
NATIONAL AQUACULTURE ASSOCIATION
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January 10, 1998

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Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive, Room 1-23
Rockville, MD 20857

Re: Docket No. 97N-0217 Discussion Draft "Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Use"

Dear Food and Drug Administration:

The National Aquaculture Association (NAA), a national not-for-profit aquaculture trade association with over 2000 members and representing a diversity of finfish and shellfish species groups, strongly supports all of the proposals presented in Docket No. 97N-0217, "Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Use." We greatly appreciate the efforts CVM has made to increase the potential for additional aquaculture drug approvals and complement them for their willingness to consider new methods of drug availability. The central issues with all of these proposals is whether human, animal or environmental safety would be compromised by their immediate implementation. We have carefully examined each proposal and conclude they are sound and would not increase jeopardy. Greater availability of drugs, as outlined in these proposals, would in fact reduce jeopardy. We provide the following comments of support:

A. MODIFICATION OF EXTRALABEL PROVISIONS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

Will the proposed modification of extralabel provisions and suggested sunset period provide adequate and appropriate temporary relief until approved products are made available, or will it serve as a disincentive to the pursuit of approvals? Should the proposed modifications be extended to include reproductive hormones and implants?

COMMENTS: The NAA is in strong support of allowing extralabel use of medicated foods for minor animal species and uses. We also continue to strongly support the Minor Species Animal Health Coalition effort to use an expanded veterinary feed directive to control extralabel medicated feed uses. The attractiveness of their proposal is that it eliminates liability and financial concerns of the feed manufacturing industry. We agree that AMDUCA did not intend to exclude

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aquaculturally raised animals from effective use of extralabel drugs. Under most circumstances, a ten year sunset clause should prove adequate to get all of the necessary data collected for a medicated feed NADA. However, there may be unforeseen circumstances that arise complicating collection of all data within the ten year time frame. We suggest FDA retain some discretionary flexibility should this happen. The extralabel use codified in AMDUCA is intended to be controlled by the veterinary profession. We suggest that control would be just as effective by the veterinary profession in aquaculture. Additionally, a ten year clause would provide incentive for a sponsor to complete the approval process in a timely fashion. We do not see any compromise in human or environmental safety should this be instituted. It would also allow opportunity for considerable data collection potentially useful for NADA submission. We also support inclusion of reproductive hormones and implants under this provision. Because of their use in brood animals and the low volumes used, they would not pose a human safety or environmental hazard.

B. REMOVAL OF DISINCENTIVES

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

Will the suggested strategies be sufficient to remove the existing direct regulatory disincentives? Are there additional disincentives to gaining approvals that should be removed? How might this be accomplished?

COMMENTS: We are unaware of any direct regulatory disincentives as described in the proposal. However, FDA should indeed have appropriate enforcement resources and legal authority to remove drugs being marketed without FDA approval. This should apply to both major and minor animal species drugs. We believe one of the greatest disincentives for drug companies is the very high cost of obtaining drug approvals with little likelihood of financial return. As FDA correctly recognizes, most aquaculture industry's are small minimizing the opportunity for financial success by a drug company under current approval programs. While we are not aware of numerous unapproved drugs and other chemical marketed in aquaculture, the recent inception of the mandatory seafood processor HACCP program, if there is any use of unapproved drugs, should significantly curtail such use. We are concerned that liability to drug companies interested in taking a major animal drug to a minor species is not addressed as a significant disincentive. We suggest this be an item of further discussion within the affected community.

C. ENHANCEMENT OF EXISTING PROGRAMS FOR DATA DEVELOPMENT

PARTICULAR ISSUE ON WHICH FDA SEEKS COMMENT

Are there additional existing congressional research funds which could be expanded for minor use research? Would the proposed model program provide a useful supplement to

the existing NRSP-7 program? Would the proposed database be useful to parties interested in furthering the approval of minor use products? If so, how might it be developed most cost-effectively?

COMMENTS: The NAA believes that appropriations for the budgets of NRSP-7, Saltonstall-Kennedy Grant Program, and National Coastal Research Institute should be increased and should have earmarked funds for aquatic animal minor drug approvals. In addition, the Upper Mississippi Science Center, La Crosse, Wisconsin for public fish culture should be protected from budget cuts and in fact should receive additional funds to pursue aquaculture drug approvals. The Stuttgart National Aquaculture Research Center, Stuttgart, Arkansas for private aquaculture should also receive additional funds to allow the expedited development of data for aquaculture drugs under existing programs and staffs. The NRSP-7 program should include minor use drugs for non-food fish and for production purposes. A minor use data base would be useful but should not be developed at the expense of any of the other proposals.

D. INCENTIVES TO PURSUE MINOR USE DRUG APPROVALS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

Is the benefit of extended exclusivity, with respect to fostering initial approval, more important than the risk of increased drug costs that could be associated with decreased competition from generic approvals? Would it be a more significant incentive to provide for an extended period of exclusivity for all the claims of the product?

COMMENTS: We suggest it is extremely important to create incentives for drug companies to pursue minor use drug approvals. The extent of financial return on drug approval investment is a key component in the decision about seeking an NADA. Aquaculture industry's are comparatively small thus any incentive FDA or congress can provide could prove helpful. Extended exclusivity, tax credits, shorter review periods, and adding residue depletion studies to the "significant new data" category to allow greater exclusivity are all important to attracting drug companies to aquaculture. Perhaps, exclusivity and shorter review periods could be extended to major drug approvals if the company agreed to develop the drug for minor uses or species. This scenario would create an incentive for the drug company to invest in minor drug uses. Additional incentive could be provided by reducing a drug companies liability for minor animal drugs. While there is some risk in lost competition with subsequent increased costs to the aquaculturist, there is currently little incentive for drug development anyway. We believe the CVM proposals should be encouraged and are in aquaculture's long term best interests.

E. DATA SHARING BY MAJOR SPECIES NADA HOLDERS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

Is it fair to require the sharing of data? How could potential liability be ameliorated under such a data sharing system?

COMMENTS: The FD & C Act should be amended to allow CVM to consider data from major drug applications when reviewing NADAs for minor uses, once the drug is in the generic classification, has been abandoned or has been withdrawn. We suggest that the lack of available data has been a significant impediment for smaller, niche marketing drug companies to consider the aquaculture market. The requirement to share the data would be fair since the major drug company many times is not interested in minor species drugs and would not be affected. Liability could be ameliorated by placing an appropriate statement on the label of the minor drug use claim.

F. CREATION BY STATUTE OF A "MINOR USE ANIMAL DRUG" PROGRAM

PARTICULAR ISSUE ON WHICH FDA SEEKS COMMENT

Would a statutory designation of "minor use animal drug" similar to the statutory designation of "human orphan drug" be useful? Are the incentives associated with this strategy a necessary component of the overall proposed "Minor Use Animal Drug Program"?

COMMENTS: We strongly endorse the proposition of amending the FD&C Act to create a category of "minor use animal drugs" similar to the "human orphan drug" designation. The incentives associated with the proposed strategies are a significant and necessary component of the overall proposed "Minor Use Animal Drug Program."

G. CONDITIONAL DRUG APPROVAL FOR MINOR USES INVOLVING NON-FOOD ANIMALS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

Would the proposed constraints upon conditional approval provide sufficient consumer protection and still provide adequate incentive to pursue a conditional drug approval to final approval? Is the proposed process appropriately restricted to minor uses involving non-food animals?

COMMENTS: Conditional drug approvals for non-food fish should be allowed and should also include gametes, eggs, fry, and fingerlings of food fish because of the inherent withdrawal time associated with these life stages. Previously, CVM has rejected this broad classification because not enough was known about metabolism of aquatic species or the definition of fingerling for each species. This situation has changed. We believe enough data has now been generated on drug metabolism, and tissue residue distribution and depletion in aquatic animals so that informed decisions can be made. The various aquaculture industry's have already provided considerable

assistance in defining these life stages. This is a critical issue to all aquaculture industry's as we seek ways to increase drug company incentives. If these early life stages of food animals were considered non-food animals, the market for a potential drug would be significantly increased. The need for mammalian safety and residue chemistry data would also be eliminated thereby significantly decreasing the cost of an NADA. Further and more importantly, human safety would not be compromised. Additionally, several compounds of potential use to aquaculture industry's are not already approved in major animal species (e.g., water borne treatment compounds such as chloramine-T). Thus the most costly part of an NADA data package, mammalian safety data, has not been collected. It is our position that greater opportunity to gain aquaculture drug approvals would occur if (1) tolerance could be calculated differently and appropriately reflecting human consumption of aquatic animals, and (2) early life stages of food fish were considered non-food.

H. ALTERNATE APPROVAL STANDARD/EXPERT REVIEW PANELS FOR MINOR USES INVOLVING NON-FOOD ANIMALS

PARTICULAR ISSUES ON WHICH FDA SEEKS COMMENT

Will animal caretakers find drugs approved under the proposed alternate standard (with associated restrictions) acceptable? Do the affected industries have the needed expertise and/or will they be willing to fund the expert review panels? Is the proposed process appropriately restricted to minor uses involving non-food animals?

COMMENTS: We believe all aquaculture animal caretakers would find any drug legally available to use to be acceptable, regardless of the standard under which it was approved. The aquaculture industry's have the needed expertise to assess target animal safety and efficacy. It is appropriate to restrict this standard to non-food fish particularly if gametes, eggs, fry, and fingerlings of food fish are included in the definition of non-food fish. There should be no provision for deletion of a drug from this non-food fish definition if it has use in later life stages because adequate regulations and controls exist to protect public health.

I. INTERNATIONAL HARMONIZATION

PARTICULAR ISSUE ON WHICH FDA SEEKS COMMENT

Could non-governmental input facilitate equivalency determinations? Are there sufficient numbers of foreign approvals to justify establishing this program? Should the proposed differences in approval, standards, processes, and data requirements between major and minor species be included in international harmonization activities?

COMMENTS: We strongly support the establishment of a system by CVM to determine whether a foreign country's requirements and systems for animal drug approvals are equivalent. We believe non-governmental input would facilitate equivalency determinations. There are

sufficient numbers of foreign aquaculture drug approvals to establish this program, based on results from recent drug harmonization workshops. CVM could advocate that each minor animal industry identify the foreign drug approvals themselves. CVM should include the proposed differences in approval, standards, processes, and data requirements between major and minor species in its international harmonization activities. We caution that some countries may classify some aquaculture chemical differently (i.e. not a drug) than FDA. We appreciate CVM's active efforts to develop international harmonization programs and their support of an upcoming international drug harmonization workshop in February, 1998.

The NAA greatly appreciates the opportunity to comment on these proposals and offer our assistance, should they prevail through further scrutiny, to help implement them. We encourage FDA and congress to seriously evaluate these proposals. We believe they are sound, offer tangible mechanisms to improve drug approvals for the US aquaculture industry's, and do not compromise human or environmental safety.

Sincerely,

John R. MacMillan

John R. MacMillan
Chairman, NAA Fish Health Committee

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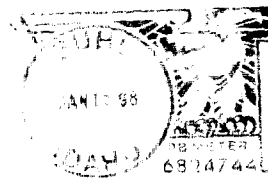

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